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Impact of nurse-targeted care on HIV outcomes among immunocompromised persons: a before-after study in Uganda

Agnes N. Kiragga, PhD[*,1], **Elizabeth Nalintya, MBChB**[1], **Bozena M. Morawski, MPH**[2], **Joanita Kigozi, MBChB MSc**[1], **Benjamin J. Park, MD**[3], **Jonathan E. Kaplan, MD**[3], **David R. Boulware, MD, MPH**[2], **David B. Meya, MBChB MMed**[1,2,5], and **Yukari C. Manabe, MD**[4]

[1]Infectious Diseases Institute, College of Health Sciences, Makerere University Kampala, Uganda [2]Division of Infectious Disease and International Medicine, Department of Medicine, University of Minnesota, Minneapolis, Minnesota [3]Division of Global HIV/AIDS (DGHA), Center for Global Health (CGH), Centers for Disease Control and Prevention, Atlanta, Georgia [4]Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland [5]School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda

Abstract

Introduction—Improving HIV outcomes among severely immunocompromised HIV-infected persons who have increased morbidity and mortality remains an important issue in sub-Saharan Africa. We sought to evaluate the impact of targeted clinic- based nurse care on ART initiation and retention among severely immunocompromised HIV-infected persons.

Methods—The study included ART-naïve patients with CD4<100 cells/μL registered in seven urban clinics in Kampala, Uganda. Data were retrospectively collected on patients enrolled from July to December 2011 (routine care cohort). Between July 2012 and September 2013, one additional nurse per clinic was hired (nurse counselor cohort) to identify new patients, expedite ART initiation and trace those loss-to-follow-up. We compared time to ART initiation and 6-month retention in care between cohorts and used a generalized linear model to estimate the relative risk of retention.

Results—The study included 258 patients in the routine care cohort and 593 in the nurse counselor cohort. The proportion of patients who initiated ART increased from 190 (73.6%) in the routine care cohort to 506 (85.3%) in the nurse counselor cohort (p<0.001). At 6 months, 62% of the routine care cohort were retained in care versus 76% in the nurse counselor cohort (p=0.001). A 21% increase in likelihood of retention in the nurse counselor cohort (relative risk 1.21, 95% CI, 1.09–1.34) compared with the routine care cohort was observed.

[*]**Corresponding author:** Agnes N. Kiragga, PhD, Infectious Diseases Institute, College of Health Sciences, Makerere University Kampala, P. O. Box 22418, Kampala, Uganda, akiragga@idi.co.ug.

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Conclusion—Implementation of targeted nurse–led care of severely immunocompromised HIV-infected patients in public outpatient health care facilities resulted in decreased time to ART initiation and increased retention.

Keywords

Retention in care; HIV; AIDS; immune-suppression; implementation science

Introduction

A key component of the plan towards an acquired immunodeficiency syndrome (AIDS)-free generation[1,2] rests on continued scale-up of antiretroviral therapy (ART). In 2013, an estimated 39% of HIV-infected persons were receiving ART in sub-Saharan Africa.[3] Linkage to ART and retention in care are of even greater importance among severely immunocompromised patients (CD4<100 cells/μL), as these patients have a high mortality risk if they do not initiate ART or if they disengage from care and treatment.[4–7] Severely immunosuppressed patients are also more likely to die in the first 6 months of ART due to opportunistic co-infections.[8–10] They still represent a significant proportion of ART initiators despite increasing availability of ART.[11,12]

There are several sequential requirements for ART scale-up: HIV-infected persons must know their status, enroll into care, initiate ART, and be retained in long-term HIV care. A recent systematic review showed considerable attrition of patients along the HIV testing to treatment cascade in Africa.[13] Only 59% (range: 35% – 88%) of patients were retained from HIV testing to receipt of CD4 count results or clinical staging, 68% (range: 14% – 84%) were retained from ART eligibility to ART initiation, and 46% (range: 31% – 95%) of initially ineligible patients were retained from staging to ART eligibility. Another systematic review by Kranzer *et al*[14], which also included studies from Africa, showed that only 66% (95% CI: 58% – 73%) of the patients who were eligible for ART (i.e., ≤350 CD4 cells/μL at the time) eventually started ART. Addressing the logistical, social, and clinical determinants of retention in care is a crucial priority in addressing the HIV epidemic,[15] as viral suppression through ART prevents new HIV transmissions with benefits to both the individual and the society as a whole.[16]

In HIV care and treatment, program monitoring and evaluation depends on the availability of regular patient follow-up, and the accuracy of outcomes that are reported in HIV care program databases.[17] However, in HIV programs worldwide, the magnitude of losses to follow-up is substantial. This is in part because most programs do not have the resources needed to contact individuals who miss appointments to ascertain their vital status, and encourage those found alive to return to care.[18–21] The expansion and decentralization of ART programs, combined with non-electronic medical record systems, leads to an inability to identify patients who transfer from one center to another. The fragmentation of individual patient records and lack of death registries also results in the erroneous categorization of patients as lost to follow-up who are actually dead, particularly among those with advanced AIDS.

As part of an operational research program, nurse-counselors were employed in the clinics, actively identified all immunosuppressed HIV patients with CD4<100 cells/μL, and were responsible for initiating them on ART and encouraging them to return for follow-up. We sought to measure the impact of assigning a nurse counselor to this severely immunosuppressed urban, outpatient population on ART initiation and retention in care within 6-months.

Methods

Ethics statement

The study and use of data was reviewed and approved by the Institutional Review Boards of the Joint Clinical Research Center, Johns Hopkins University, University of Minnesota, United States Centers for Disease Control and Prevention, and the Uganda National Council for Science and Technology. The data for this study were collected from clinic databases used for routine reporting. Patients provided consent for care, and no personal identifiers were made available to the researchers during the analysis.

Study settings

This study included patients who registered for HIV care at seven urban public, Kampala Capital City Authority (KCCA) clinics in Kampala, Uganda. These ART clinics are supported by the Infectious Disease Institute in Kampala, a private, not-for-profit organization providing care to people living with HIV at these public clinics.

Study population

Routine care cohort—Study subjects in the routine care cohort were patients who registered for care at any of the KCCA clinics between July 2011 and December 2011, were ART-naïve and had CD4<100 cells/μL. Standard of care for all HIV positive persons included ART assessment, and initiation for CD4 T cell count ≤ 350 cells/μL, according to the Ugandan HIV guidelines. Patients received a baseline CD4 count and then every 6 months. Patients returned monthly for prescription refills and a brief follow-up visit to address emerging issues. Counsellors performed a baseline intake followed by 2 additional counselling sessions to assess readiness and encourage adherence. Viral load testing was not part of standard of care until 2015. During this routine care period, no specific healthcare provider was assigned to severely immunosuppressed HIV patients, and available staff managed their care. In this cohort the clinic staff did not actively trace patients who were lost to follow-up. However, a list of these patients who met the definition of lost to follow up were contacted in July 2012 through telephone calls or home visits if the address was available.

Nurse counselor cohort—The nurse counselor cohort included patients enrolled in care as part of an implementation science program to introduce cryptococcal antigen screening among patients with CD4 counts <100 cells/μL (Operational Research for Cryptococcal Antigen Screening (ORCAS) trial, Clinicaltrails.gov identifier: NCT01535469). This prospective stepped-wedge trial began in July 2012, and patients were followed for 6-months post CD4 testing. During the initial prospective observational phase prior to the

incremental roll out of cryptococcal antigen screening in the ORCAS trial, one additional research nurse per clinic was specifically tasked with identifying patients who were ART-naïve and had recent CD4<100 cells/μL. Nurse counsellors enrolled were selected on the basis of having had prior experience is research studies and having worked in a clinical setting. The nurses were then trained in the clinical assessment of the patients in collaboration with the existing health center clinician who attended to the patient. They also received training on assessment of ART initiation, assessment of opportunistic infections, as well as tracing of patients who dropped out of care.

The nurse counselors were responsible for guiding these patients through the clinic system, expediting ART initiation, and ensuring follow-up monthly for six months. All other aspects of care were similar to the standard of care offered in the routine care cohort. Tracing of patients who were lost to follow up was actively performed by the nurse counselors through telephone calls and home visits. Patients provided their primary telephone numbers and address. Nurses used these data to trace the patients who did not return to the clinic for care or missed ≥2 consecutive visits with a telephone call or home visits when an address was provided. The nurses ensured that clinical/medical officers evaluated patients, and patients were asked to contact the nurses directly if they experienced symptoms of illness or adverse reactions to ART.

Variable definition, data sources and statistical analysis—Data for the routine care cohort (patients with CD4<100 cells/μL) were extracted from routinely collected chart data from the ART clinic and entered into a separate study database. Data on process indicators of care were recorded, such as time from clinic registration to CD4 blood draw, and time from CD4 blood draw to ART initiation. Retention in care and vital status at 6 months post-registration were collected. The cut-off of six months was chosen because mortality and attrition are highest in the first 6 months after ART initiation.[22] CD4 count testing was generally performed at the time of registration into HIV care.

Analyses of categorical and continuous variables across cohorts were conducted using Chi-square and Mann-Whitney U tests. We used a generalized linear model to estimate the relative risk of retention in care in the nurse counselor cohort versus routine care. In the model we adjusted for gender, CD4 cell count, and WHO clinical stage at enrollment. Robust standard errors were used to account for correlation between clinics. All statistical analysis was conducted in Stata 12.1 (StataCorp, College Station, TX).

Results

Analyses included 258 patients in the routine care cohort and 593 in the nurse counselor cohort for whom 6 months had elapsed since enrolment into care. In both cohorts, the median age was 32 [interquartile range (IQR): 27, 38.5] years, and 55% were women (Table 1). The median CD4 T-cell count at baseline was slightly lower in the routine care cohort at 34 [IQR: 12, 63] cells/μL compared to 42 [IQR: 17, 71] cells/μL in the nurse counselor cohort, p=0.002. The proportion with WHO clinical stage III or IV at staging decreased from 54% to 40% between the two time periods (p<0.001), although all persons had CD4<100 cells/μL.

Indicators of care

With implementation of the nurse counselor, the proportion of patients who initiated ART increased from 190 (73.6%) in the routine care cohort to 506 (85.3%) in the nurse counselor cohort (p<0.001). In addition, time from CD4 blood draw to ART initiation decreased from a median of 42 [IQR: 28, 56] days in the routine care cohort to 34 [IQR: 22, 46] days in the nurse counselor cohort (p<0.001). The number of scheduled follow-up CD4 measurements also improved; among the patients retained in care in the routine care cohort, 24% (39/160) received a CD4 count test at 6 months versus 53% (240/450) in the nurse counselor cohort. The mean CD4 increase (standard deviation) at six months was +88 (±157) cells/μL in the routine care cohort, compared with +133 (±120) cells/μL in the nurse counselor cohort (p=0.028).

Retention in care

In order to ascertain the retention of patients in both cohorts, tracing of all patients who were lost to follow-up was performed and a final outcome established. Within the routine care, 62% (160/258) of patients were alive and in HIV care after 6 months. In comparison, in the nurse counselor cohort, 76% (450/593) were alive and in HIV care and on ART after 6 months. In the routine care cohort, 8.9% of the cohort was confirmed dead at 6 months, compared to 14.2% in the nurse counselor cohort. The proportion of patients who were lost to follow-up and not contactable after tracing efforts was higher among the routine care cohort 26.4% (68/258; 95%CI 1.0–32.2) compared with the nurse counselor cohort 7.8% (46/593; 95%CI 5.7–10.2) (p< 0.001) (Table 2). Adjusting for potential confounders in the generalized linear model which included age, gender, CD4 count at enrolment, and WHO clinical staging, there was a 21% increase in likelihood of retention in care in the nurse counselor cohort (relative risk=1.21, 95% CI, 1.09 – 1.34, p<0.001) and a lower likelihood of retention in persons with WHO stage III or IV disease (relative risk= 0.80, 95% CI 0.73 – 0.88) (Table 3).

Discussion

Our study demonstrates the value of targeted care for severely immunocompromised patients, who are at higher risk for mortality in the first months of HIV care. We demonstrated a 21% improvement in retention in care with the addition of a nurse counselor who was responsible for facilitating initial HIV care for this high-risk population. This improvement in retention in care was likely partially related to the decrease in time from enrolment to ART initiation (approximately one week less with a nurse counselor). Delay in ART initiation is a known key risk factor for mortality.[23] There are few other documented interventions that decrease the time from enrolment to ART initiation. In Mozambique, Jani *et al* have shown that time to ART initiation dropped from 48 (IQR 34–80) to 20 days (IQR 10–31, p<0.001) with the use of point-of-care CD4 testing and nurse follow-up with the patient.[24] A recent meta-analysis demonstrated that task shifting, in which nurses initiated and provided HIV follow-up care instead of medical doctors, reduced mortality through improved linkage to and retention in care.[25]

However, expediting HIV treatment alone does not explain the improved retention in care. In the nurse counselor cohort, the same nurse counselor saw patients at all follow-up visits in conjunction with medical officers. This personalized provider-patient relationship in an otherwise impersonal public-sector HIV treatment program should not be overlooked as a strategy to improve retention in care. A recent randomized clinical trial in urban clinics in sub-Saharan Africa also showed ~30% relative reduction in all-cause mortality in patients with CD4<200.[26] Patients in the intervention arm of this trial received prompt ART initiation, TB screening with Xpert MTB/RIF, and cryptococcal antigen screening (and preemptive treatment of positives), coupled with a short period of community adherence support. This adherence support similarly created personalized support of high-risk patients.

Other interventions that have demonstrated improved retention include short messaging services through mobile phones and voucher-based incentives. A randomized clinical trial in Kenya reported lower risk of non-adherence to ART medication in the arm that received the short messaging services compared to the control arm.[27] In India, vouchers that were redeemable for food or household goods have also been shown to be effective in improving linkage to and retention in HIV care.[28] However, each patient living with HIV is unique, and measures that work for one patient may not work for another.

In our study, we have shown an increase in 6-month retention with the institution of a dedicated nurse to target care for severely immunosuppressed patients. Although our study concentrated on patients with CD4<100, this model could be applied to other specific groups of ART eligible patients. This intervention has cost and logistical implications that must be weighed against the potential personal and public health benefits. Comparing community-based to clinic-based retention support should be investigated further in terms of cost of implementation and scale-up. The nurse counselors in our study were responsible for navigating patients through the busy clinics and ensured that patients received all necessary clinical assessments and prescribed medication. Patients often contacted the nurse counselors whenever they were ill, and this consistent point-of-contact likely contributed to better retention. A recent editorial emphasizes the need for focused attention and personal contact with the same health care worker when dealing with HIV-infected patients in busy HIV clinics,[15] and indeed in our experience, patients feel comfortable and are reassured by having an identified staff liaison in busy urban clinics.

There are several limitations of this study. First, we were unable to obtain information on cause for attrition among a significant proportion of the patients in the routine care cohort. The proportion of patients who were known to have died was higher in the nurse counselor cohort likely due to better ascertainment. Second, the study relied on routinely collected data in the routine care cohort versus the nurse counselor cohort, which used a combination of routine and nurse collected data. Third, we did not measure viral loads to determine if improved retention in care was associated with improved overall HIV viral suppression; this should be studied in the future. Furthermore, the possibility of a calendar effect with possible confounding by an unmeasured improvement in quality of care in the later time period could have led to an improvement in the results.

Despite its limitations, this study demonstrates that nurse counselors dedicated to immunosuppressed patients initiating ART in busy public sector HIV care facilities can effectively facilitate care of high-risk patients and improve retention in HIV care. This role could be potentially effectively task-shifted to community volunteers, expert patients or community health workers. This is in line with the WHO recommendations of task shifting for HIV care, and has implications of other outcomes such as quality of life, as was reported in Cameroon[29–31]. The presence of the nurse led to improvements in overall care given to high-risk patients in low-resource urban clinics in Uganda. Further prospective studies are needed to establish best practices and cost effectiveness of this strategy. As the CD4 threshold for ART initiation increases, this strategy should also be tested for all ART-eligible patients including those with higher CD4 cell counts who are newly entering into HIV care.

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Table 1

Baseline demographics among HIV-infected patients in the routine care and nurse counselor cohorts

Variable	Routine care N = 258	Nurse counselor N = 593	P value
Women	142 (55.0%)	327 (55.1%)	0.978
Age in years	32 (27, 39)	32 (27, 38)	0.431
CD4 count, cells/μL	34 (12, 63)	42 (17, 71)	0.002
Body Mass Index, kg/m^2	19.9 (18.1, 21.8)	19.8 (18.0, 22.2)	0.564
WHO III/IV clinical stage	140 (54.3%)	239 (40.3%)	<0.001

Data are N (%) or median (interquartile range).

N=number. WHO=World Health Organization. Body Mass Index missing for 176 patients in the routine cohort, and on 16 patients in the nurse counselor cohort

Table 2

Patient outcomes 6 months after entry into HIV care

Six month outcome	Routine care N = 258	Nurse counselor N = 593	P Value
Alive-in-Care, n Proportion (95% CI)	160 62.0 (55.8 – 67.9)	450 75.9 (72.2 – 79.3)	<0.001
Dead, n Proportion (95% CI)	23 8.9 (5.7 – 13.1)	84 14.2 (11.5 – 17.2)	
Transferred care, n Proportion (95% CI)	7 2.7 (1.1 – 5.5)	13 2.2 (1.2 – 3.7)	
Lost to follow-up, n Proportion (95% CI)	68 26.4 (1.0 – 32.2)	46 7.8 (5.7 – 10.2)	

Table 3

Baseline factors associated with >6 month retention in HIV care

Variable	Risk Ratio (95% CI)	P Value
Routine cohort	Reference	
Nurse counselor cohort[§]	1.21 (1.09 – 1.34)	<0.001
Age in years		
14 – 27	Reference	
28 – 32	0.99 (0.92 – 1.08)	0.955
33 – 38	0.94 (0.83 – 1.06)	0.287
≥39	0.94 (0.84 – 1.06)	0.334
Gender		
Men	Reference	
Women	1.01 (0.92 – 1.09)	0.928
CD4 count at baseline		
< 50 cells/μL	Reference	
≥ 50 cells/μL	0.99 (0.92 – 1.08)	0.893
WHO clinical stage		
I–II	Reference	
III–IV	0.80 (0.73 – 0.88)	<0.001

WHO=World Health Organization. CI=Confidence interval.

[§]The analysis was adjusted for gender, CD4 counts, and WHO stage